# CANADIAN JOURNAL OF RESEARCH

VOLUME 28 JANUARY, 1950 NUMBER 1


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# CHEMICAL SCIENCES

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# Canadian Journal of Research

*Issued by* THE NATIONAL RESEARCH COUNCIL OF CANADA

VOL. 28, SEC. B. JANUARY, 1950 NUMBER 1


## THE ACTION OF ZINC ON α,β-DIBROMOPROPIONYL HALIDES[1]


BY E. H. CHARLESWORTH AND H. J. ANDERSON



### Abstract

A vigorous reaction occurs between zinc filings and a solution of α,β-dibromopropionyl bromide in absolute ether. The principal organic products of the reaction are ethyl acrylate and ethyl bromide. Suggested steps in the reaction are described. The α,β-dibromopropionic acid from which the acid halides were made was obtained by oxidation of β,γ-dibromopropyl alcohol. Treatment of β-bromopropionic acid in the Hell–Volhard–Zelinsky reaction failed to accomplish bromination in the α-position, only β-bromopropionyl bromide being isolated.


### Introduction

During some war time research on ketenes a nonketenic liquid* of molecular formula $C_5H_8O_2$ was obtained by the action of zinc filings on a solution α,β-dibromopropionyl bromide in absolute ether. This was the general method introduced by Staudinger and his coworkers (7, 8, 9) for the production of ketoketenes $R_2C=C=O$, but it apparently has never been successfully used in the preparation of pure samples of ketene itself and aldoketenes $R-CH=C=O$. Hurd, Cashion, and Perletz (2) report difficulty in repeating the work of Staudinger and Klever (8).

No trace of ketenic material has been isolated in this work. The nonketenic liquid mentioned above has been re-examined recently and has been identified as ethyl acrylate. Accompanying the ethyl acrylate (55% yield) were smaller amounts of ethyl bromide (6 to 8%) and hydrogen bromide (42%). The following steps are considered to represent the possible courses of the reaction and in most cases are substantiated by the work of other authors as indicated.

1. $BrCH_2-CHBr-COBr + Zn \longrightarrow CH_2=CH-COBr + ZnBr_2$
2. $C_2H_5-O-C_2H_5 \xrightarrow{ZnBr_2} C_2H_5OH + C_2H_4$
3. $BrCH_2-CHBr-COBr + C_2H_5OH \longrightarrow BrCH_2-CHBr-COOC_2H_5 + HBr.$
4. $C_2H_5OH + HBr \longrightarrow C_2H_5Br + H_2O$
5. $C_2H_4 + HBr \longrightarrow C_2H_5Br$
6. $BrCH_2-CHBr-COOC_2H_5 + Zn \longrightarrow CH_2=CH-COOC_2H_5 + ZnBr_2$
7. $CH_2=CH-COBr + C_2H_5OH \longrightarrow CH_2=CH-COOC_2H_5 + HBr$

Step 1 need take place only to a very limited extent, since the zinc bromide is a catalyst and since more is formed as the reaction progresses (Step 6).


[1] *Manuscript received in original form June 7, 1949, and, as revised, October 31, 1949. Contribution from the Department of Chemistry, University of Manitoba, Winnipeg, Manitoba.*


* *Isolated in 1944 by J. E. Sinder.*

Step 1 must be comparatively slow, as indicated by the necessity of continued agitation and warming for at least half an hour. Once started however, the reaction had to be controlled by cooling. The reaction can also be initiated by dissolving a small drop of water or alcohol in 10 ml. of absolute ether and adding 1 ml. of this solution to the reaction mixture.

Steps 2 to 5 are supported by the work of Underwood and Toone (10) and Underwood and Wakeman (11), who have shown that a very small amount of zinc chloride can cause ether to break down into alcohol and ethylene, with subsequent esterification of the acid chloride and conversion of the alcohol to ethyl chloride.

The presence of hydrogen bromide was proved by the isolation of aniline hydrobromide in an aniline trap. Step 6 is in agreement with the work of Michael and Schulthess (4), who, as early as 1891, showed that metallic zinc will remove vicinal halogens from ethyl α,β-dibromopropionate, yielding ethyl acrylate.

The α,β-dibromopropionyl halides used were prepared by the oxidation of β,γ-dibromopropyl alcohol with nitric acid to the corresponding dibromo acid, followed by treatment with either thionyl chloride or phosphorus and bromine.

Attempts to produce α,β-dibromopropionyl bromide by the Hell–Volhard–Zelinsky reaction on β-bromopropionic acid gave β-bromopropionyl bromide, almost exclusively. Apparently halogenation in the α-position did not occur to any extent under these conditions.

## Experimental

*α,β-Dibromopropionyl Bromide*

α,β-Dibromopropionic acid (46 gm.) was mixed with red phosphorus (2 gm.), and bromine (42 gm.) was added slowly with cooling. On completion of the reaction the flask was allowed to stand several hours at room temperature. The excess bromine was driven off by warming and the residue fractionally distilled. The portion collected at 79° to 86° C. (10 mm.) on redistillation gave the acid bromide (49 gm.) as a clear straw colored liquid boiling at 79° to 80° C. (10 mm.). It was characterized by conversion to previously listed esters of the parent acid and to the unlisted anilide which crystallized from 50% alcohol as fine white needles, melting at 155° to 156° C. Found: Br, 52.26%. Calc. for $C_9H_9ONBr_2$: Br, 52.15%.

*β-Bromopropionyl Bromide*

β-Bromopropionic acid (32 gm.), red phosphorus (2 gm.), and bromine (42 gm.) were treated in the manner described above. Distillation gave β-bromopropionyl bromide (28 gm.) boiling at 68 °to 70° C. (12 mm.). Found: Br, 74.61%. Calc. for $C_3H_4OBr_2$: Br, 74.07%. It was characterized by the preparation of several derivatives of the parent acid not previously listed.

The *anilide* crystallized from water in white needles, melting at 119° to 120° C. Found: Br, 35.25%. Calc. for $C_9H_{10}ONBr$: Br, 35.10%.

*n-Propyl β-bromopropionate*: b.p. 76° to 78° C. (10 mm.); $n_D^{20}=1.467$.

*Dehalogenation Reactions*

(*a*) *Using α,β-Dibromopropionyl Bromide*

The reaction was carried out in a three-necked, round-bottomed flask, equipped with stirrer, reflux condenser, dropping funnel, and inlet tube for an inert atmosphere of nitrogen. An outlet tube from the condenser was attached to an empty wash bottle, followed by a wash bottle containing aniline. A solution of α,β-dibromopropionyl bromide (25 gm.) in absolute ether (100 ml.) was added to zinc filings (7.5 gm. B.D.H. Analar.). After the contents of the flask had been stirred and warmed for about 30 min. a vigorous reaction set in which was controlled by cooling. On completion of the reaction, the mixture was poured into excess dilute ammonia solution, thoroughly stirred, and the ethereal layer separated, dried, and distilled. By careful distillation, through an efficient column, a liquid (4.8 gm. 55% yield) boiling at 99° to 100° C. (740 mm.) and possessing a strong characteristic odor was obtained. Found: C, 61.8; H, 7.66%; mol. wt., 93.8; $n_D^{20}=1.410$. Calc. for $C_5H_8O_2$: C, 60.0; H, 8.0%; mol. wt., 100. The liquid was characterized as ethyl acrylate by conversion into the *p*-toluidide of acrylic acid, m.p. 140° to 141° C., by the method of Koelsch and Tenenbaum (3) and into the 3,5-dinitrobenzoate of ethyl alcohol, m.p. 93° C., by the method of Renfrow and Chaney (6). The ester and the two solid derivatives described were identical in every respect with authenic samples prepared from acrylic acid made by the method of Moureu, Murat, and Tampier (5) from β-bromopropionic acid.

Careful refractionation of the higher ether runnings gave a liquid (b.p. 37° to 40° C.) containing ethyl bromide. Treatment of this liquid with magnesium, followed by α-naphthyl isocyanate according to the directions of Gilman and Furry (1) gave propion-α-naphthalide (0.35 gm.) melting at 124° to 126° C. No depression was noted on a mixed melting point with an authenic specimen. On the assumption of the usual 25% to 30% yield of the naphthalide from the alkyl halide under these conditions, the amount of ethyl bromide present in the liquid would be 0.55 to 0.75 gm., a 6 to 8% yield on the basis of all hydrogen bromide forming ethyl bromide.

From the aniline trap a crystalline solid separated, and dilution with benzene gave a little more. This compound (6.4 gm.) on washing with ether and after crystallization from water melted at 285° to 289° C. It was identified as aniline hydrobromide and represents a 42% yield of hydrogen bromide on the basis of Reaction 3. The rest either reacted to form ethyl bromide (6 to 8%) or remained dissolved in the reaction mixture. On treatment with bromine water, the aniline hydrobromide gave 2,4,6-tribromoaniline, m.p. 118° to 119° C.

(*b*) *Using α,β-Dibromopropionyl Chloride*

When this substance was treated with zinc according to the foregoing directions ethyl acrylate was obtained as before. The ethyl chloride, being more volatile than the ethyl bromide, passed through the condenser and was caught in the aniline trap along with hydrogen chloride. After several crystallizations from alcohol and water, a product melting from 150° to 170° C. was obtained. This was considered to be a mixture of the hydrochlorides of aniline and ethyl aniline, but was not separated or investigated further.

(*c*) *Using β-Bromopropionyl Bromide*

When this substance was treated with zinc according to the foregoing directions a 60% yield of ethyl β-bromopropionate was obtained.

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# THE THERMAL DECOMPOSITION OF STYRENE–BUTADIENE POPCORN POLYMER[1]

By J. Halpern[2] and C. A. Winkler


## Abstract

At temperatures of the order of 250° C., popcorn polymer undergoes decomposition to soluble polymer. The reaction is catalyzed by peroxides present in the popcorn when the latter is formed. These peroxides may be removed by extracting the polymer with benzene. The kinetics of both the catalyzed and purely thermal solubilization reactions were investigated. The rates of both reactions are first order, the catalyzed degradation having a higher activation energy and a higher frequency factor. The rate of the thermal reaction decreases and its activation energy increases with increasing butadiene content of the polymer. A linear relation between the activation energy and the log of the frequency factor, for the decomposition of popcorn polymers of different butadiene contents, was observed. The results indicate that the rate of solubilization is determined by the activation energy of the bond scission process, and is independent of the degree of cross-linking of the polymer.


## Introduction

The copolymerization of styrene with relatively small amounts of butadiene yields an insoluble polymer of very low swelling index (9). Because of its opaque appearance and proliferative activity it has come to be known commonly as *popcorn* polymer. The kinetics of its formation have been studied in this laboratory (1), but these studies yielded little information about the structure of the network formed, and the relation between the insoluble polymer and soluble copolymers which can be obtained from the same monomers. The present paper describes an effort which has been made to obtain such information by a study of the thermal decomposition of popcorn polymer into soluble polymer.

## Experimental Methods

### *The Preparation of Popcorn Polymer*

The styrene and butadiene used in the preparation of popcorn polymer were supplied by the Polymer Corporation, Sarnia. The butadiene was passed through 2 *N* sodium hydroxide to remove the inhibitor (*t*-butylcatechol), after which it was dried over activated alumina and stored at −78° C. The styrene was distilled under reduced pressure, and stored at 0° C. Both materials were used within a few days after purification.

Popcorn polymer was prepared in the first instance by allowing a monomer mixture of the desired composition to polymerize at 50° C. in the absence of air or catalysts. Under these conditions popcorn formed after an induction

[1]*Manuscript received June 7, 1949.*
*Contribution from the Physical Chemistry Laboratory, McGill University, Montreal, Que., with financial assistance from the National Research Council of Canada, through the Associate Committee on Synthetic Rubber.*
[2]*Holder of a Fellowship under the National Research Council of Canada.*

period of about one week. This popcorn was used as seed in subsequent preparations. When a small amount of this material was added to the monomer, the induction period noted above was not observed, and the amount of soluble polymer, which formed along with the popcorn by normal polymerization, was reduced. All the popcorn polymer used in the decomposition studies was prepared from seeded monomer.

One-tenth gram of seed, of the same composition as the monomer mixture being used, was weighed into a Pyrex reaction tube of about 15 ml. capacity, 5 ml. of styrene added, and the tube cooled to −78° C., and evacuated. Butadiene was then condensed into the tube from a calibrated volume until the desired butadiene : styrene ratio was obtained, as determined by pressure measurements in the calibrated volume, before and after condensation. The reaction tubes were sealed off, and allowed to stand in a thermostat at 50° C. for one week. Since the yield of popcorn obtained was about 95%, (the remainder being soluble polymer), its composition may be assumed to be the same as that of the original monomer solution. Different preparations of popcorn polymer of given butadiene: styrene ratio gave reproducible results in subsequent decomposition studies.

*The Thermal Decomposition of Popcorn Polymer*

In the first experiments the popcorn, after preparation, was decomposed in the sealed tubes in which it had been prepared. This made it unnecessary to expose the polymer to air, the presence of which was found to bring about an oxidative degradation, more rapid than the purely thermal decomposition. The tubes were placed in a thermostatically controlled furnace, and withdrawn after recorded intervals of time, to determine the soluble polymer content. A sample of the partially decomposed polymer was refluxed in about 50 ml. of benzene for four hours, after which the benzene–polymer mixture was transferred to a glass-stoppered graduated cylinder. The insoluble polymer (gel) was allowed to settle for 24 hr. and its volume, as well as that of the over-all mixture, was noted. The concentration of soluble polymer (sol) in the supernatant liquid, determined by evaporating an aliquot, was found to be approximately the same as its concentration in the solvent held in the residual insoluble network. From the data obtained, the per cent soluble polymer and the swelling index of the remaining insoluble polymer were calculated. The soluble polymer content determined in this manner is estimated as being accurate to within 5% and the swelling index to within 10%.

In most of the experiments the popcorn was extracted (to remove soluble polymer and peroxides) prior to decomposition. The extraction was accomplished by refluxing the popcorn in benzene at 80° C. for the desired length of time, about 50 ml. of benzene being used for each 10 gm. of polymer. The solution was filtered off and the insoluble residue washed several times with benzene. After the last traces of solvent had been removed by continued pumping at low pressures, samples of the popcorn were introduced into Pyrex

tubes which were then thoroughly evacuated and sealed off. Decomposition of the material and subsequent analysis of the products were as outlined previously.

*Peroxide Analysis*

The peroxide content of the benzene extract from the popcorn polymer was determined by the method of Robey and Wiese (7). An aliquot of the solution was diluted with a standard alcohol–chloroform solution of ferrous sulphate and potassium thiocyanate. The intensity of the color developed was compared in a Fisher Electrophotometer with the color intensities of a series of standard solutions of benzoyl peroxide treated in a similar way. Such an estimate of the amount of peroxides extracted from the polymer cannot be regarded as better than approximate, since some of the peroxide was probably decomposed during the extraction. In addition, the development of a maximum color intensity with time made comparison difficult. However, the results are adequate for comparative purposes.

## Experimental Results

. Popcorn polymer containing 3.97 mole% butadiene was decomposed in the same tubes in which it had been prepared, at four temperatures between 230° and 250° C. The results are shown in Fig. 1. A plot of log (90 − %

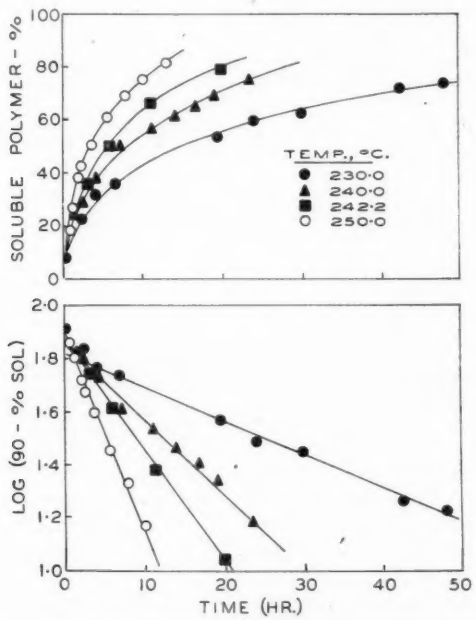


FIG. 1. *The decomposition of unextracted popcorn polymer containing 3.97 mole% butadiene.*

soluble polymer) against time is shown in the same figure. The series of straight lines obtained indicates a first order reaction with an end point of 90%. However, since prolonged heating did lead eventually to complete solubilization, this end point must be only apparent, and its significance is not clear. Measurements in the region of more than 80% decomposition probably have little meaning, since the remaining gel was highly swollen and did not settle readily.

First order rate constants were determined from the slopes of the lines in Fig. 1. When log $k$ was plotted against $1/T$, a fairly good Arrhenius line

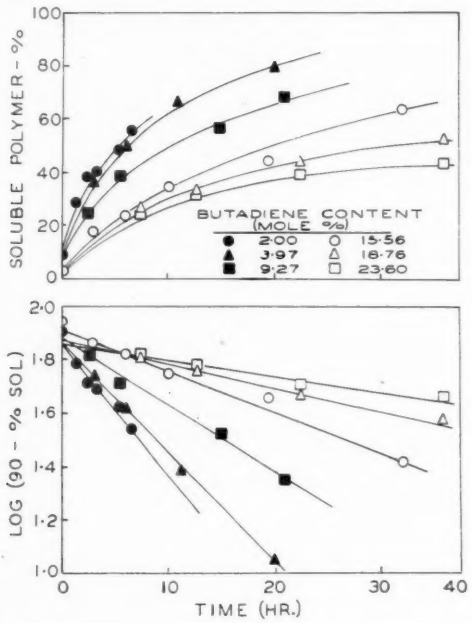


FIG. 2. *Rate curves for the decomposition of unextracted popcorn polymer of different butadiene contents. Temperature, 242.2° C.*

was obtained, corresponding to an activation energy, $E$, of 47.8 kcal. per mole. The frequency factor, $A$, of the reaction, calculated from the Arrhenius equation, is $9.4 \times 10^{17}$ hr$^{-1}$.

The effect of the butadiene content of popcorn polymer on its rate of decomposition was determined. Popcorn polymers with butadiene contents ranging from 2.00 to 23.60 mole% were decomposed at 242.2° C., giving the results shown in Fig. 2. The decomposition rate is plotted as a function of the butadiene content in Fig. 3.

The swelling index of the insoluble polymer was found to increase during the reaction from an initial value of about 10 cc. per gm. to about 100 cc.

per gm. at 80% decomposition. The data are not given, since the measurements of the swelling index in these experiments were not satisfactorily reproducible.

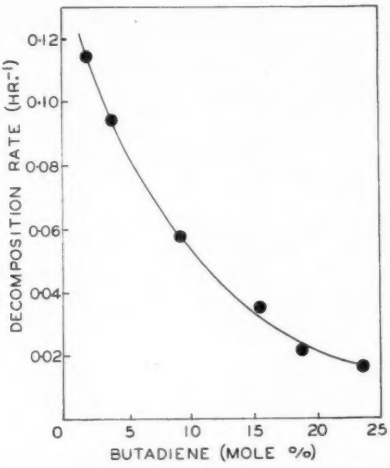


FIG. 3. *Relation between the butadiene content of unextracted popcorn polymer and its rate of decomposition. Temperature, 242.2° C.*

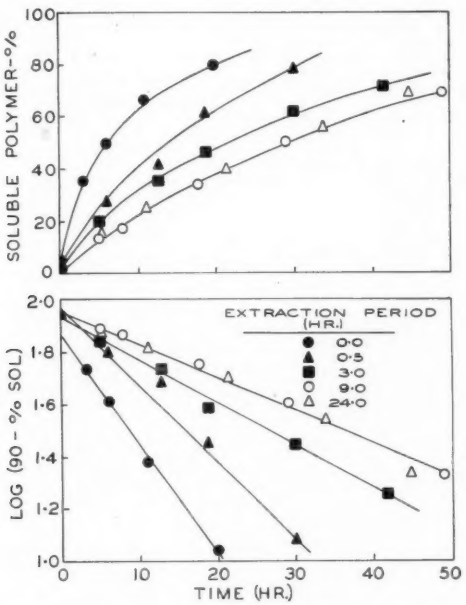


FIG. 4. *Rate curves for the decomposition of popcorn polymers after extraction for different lengths of time. Butadiene content, 3.97 mole%. Temperature, 242.2° C.*

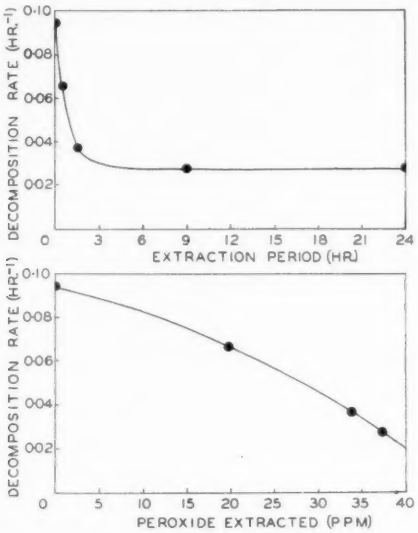


FIG. 5. *Effect of extraction on the rate of decomposition of popcorn polymer. Butadiene content, 3.97 mole%. Temperature, 242.2° C.*

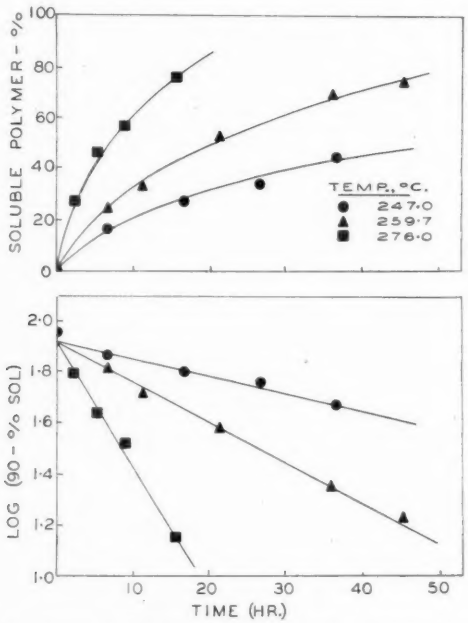


FIG. 6. *Typical rate curves for the decomposition of extracted popcorn polymer. Butadiene content, 23.60 mole%. Extraction period, 48 hr.*

An attempt was made to obtain more uniform starting material, hence better reproducibility, by extracting the popcorn polymer before decomposing it, with a view to removing the variable small amounts of soluble polymer present in the initial preparation. Preliminary experiments showed, however, that prior extraction of the popcorn polymer greatly reduced its rate of decomposition. A study of this effect was therefore made.

Popcorn polymer containing 3.97 mole% butadiene was extracted for different periods of time and its rate of decomposition determined at 242.2° C. The results are shown in Figs. 4 and 5. The rate of decomposition decreased regularly as the extraction time was increased, reaching a limiting value after about five hours. This indicated that there was some material present in the popcorn which catalyzed the decomposition and which was removed by the extraction. Studies of the formation of popcorn polymer have indicated the presence of peroxides in popcorn (4). This suggested that peroxides might be responsible for the observed catalytic activity.

This conclusion is supported by the results in Fig. 5, obtained by analyzing the extract solutions for peroxides. The rate of decomposition is seen to fall off regularly as the amount of peroxide extracted from the popcorn is increased. Noting that the peroxide determinations for the longer extraction periods are probably low, because of peroxides destroyed during the extraction, the relation would seem to be approximately linear. It would appear

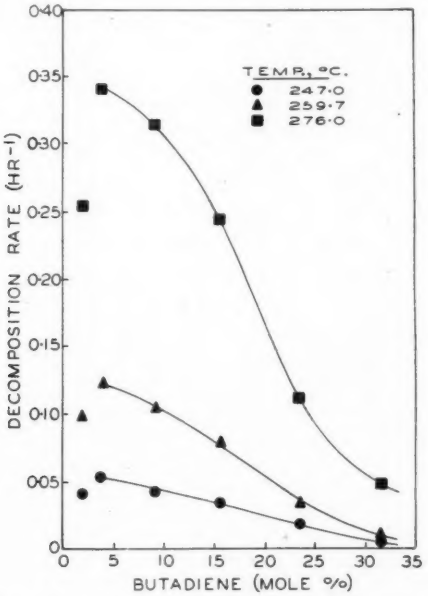


FIG. 7. *Relations between the butadiene content of extracted popcorn polymer and its rate of decomposition.*

then that the decomposition of unextracted popcorn polymer is a composite reaction, proceeding partly by a thermal rupture of the bonds in the network, and partly by a peroxide catalyzed degradation. A similar catalytic activity of peroxides has been observed in studies on the degradation of polystyrene (5).

To obtain results which could be more readily and usefully interpreted, it seemed advisable to study the purely thermal decomposition. Popcorn polymers with butadiene contents ranging from 2.00 to 31.65 mole% were completely freed of peroxides by extracting for 48 hr., and their rates of decomposition determined at 247.0°, 259.7°, and 276.0° C. Typical results (for popcorn containing 23.60 mole % butadiene) are shown in Fig. 6. In Fig. 7 the rates are plotted as functions of the butadiene content, for the different temperatures. At each temperature the rate is seen to fall off regularly with increasing butadiene content in the range of 3.97 to 31.65 mole % butadiene. The low values for the polymer containing 2.00 mole % butadiene may be due to experimental error in preparing the popcorn.

Good Arrhenius lines were obtained for the different popcorn polymers. The activation energies, $E$, calculated from the slopes of these lines are plotted as a function of the butadiene content in Fig. 8. $E$ is seen to increase with increasing butadiene content of the polymer.

The rate of increase of the swelling index of the insoluble polymer during the decomposition was also determined. In Fig. 9, typical relations between the swelling index and the amount of soluble polymer formed are shown for two of the popcorn polymers at the three temperatures used. Similar

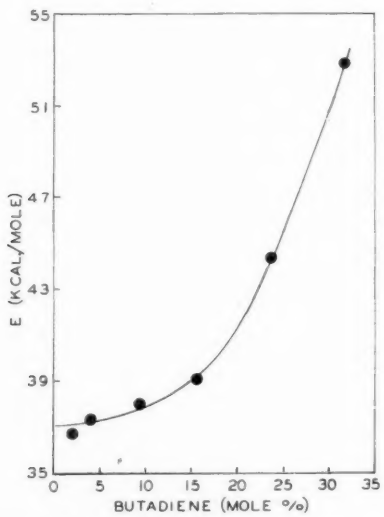


FIG. 8. *Relation between the butadiene content of extracted popcorn polymer and the activation energy of the decomposition reaction.*

curves were obtained for the other polymers of intermediate butadiene content. These lie between the two curves shown, but their relative positions bear no particular relation to the butadiene contents of the polymers.

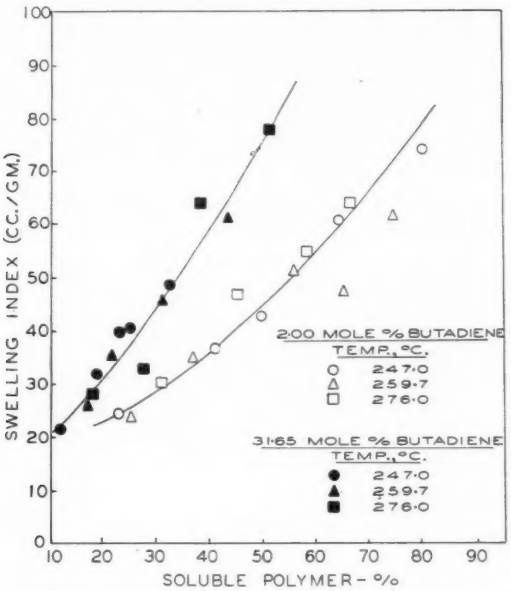


FIG. 9. *Typical relations between the swelling index and the amount of soluble polymer.*

## Discussion

Interpretation of the results for the decomposition of unextracted popcorn polymer is complicated by the fact that the rate of the reaction is dependent upon the peroxide content of the polymer.

It is interesting, however, to compare the activation energies and frequency factors for the decomposition of unextracted and extracted polymer of the same butadiene content. For popcorn polymer containing 3.97 mole% butadiene, the rate of decomposition before extraction is given by,

$$k = 9.4 \times 10^{17}\, e^{-47,\,800/RT}$$

and the rate after extraction by,

$$k = 2.0 \times 10^{14}\, e^{-37,\,400/RT}\,.$$

The effect of extraction is therefore to decrease both the frequency factor and the activation energy of the reaction. The observed decrease in rate resulting from extraction indicates that the change in frequency factor has the predominating influence. The catalytic effect of the peroxides thus

appears to be due to a reaction of higher frequency factor rather than of lower activation energy, accompanying the purely thermal destruction of the network.

Since extracted popcorn polymers are free from peroxides, their rates of decomposition should be functions only of the butadiene : styrene ratio and the structural characteristics of the network concerned. Most of the bonds in the popcorn polymer network are presumably between molecules of styrene, the component present in excess. In addition, however, there must be bonds involving butadiene molecules. All branching and cross-linking presumably occur through such bonds.

Solubilization of the popcorn polymer may occur through random thermal cleavage of the bonds in the network. On the other hand, since the presence of butadiene in the polymer is primarily responsible for its insolubility, it is possible that the bonds involving butadiene are of particular significance in maintaining this insolubility. Scission of such bonds should then be correspondingly more effective in solubilizing the polymer.

To obtain information on this point, the variation of the rate and activation energy of the decomposition reaction with the butadiene content of the polymer was determined. However, before these data can be adequately interpreted, it is necessary to establish that the activation energy, determined from rates of solubilization, can be taken to represent the activation energy of the bond scission process upon which the solubilization depends. This in turn implies that the functional relation between the rate of solubilization and the rate of bond cleavage is independent of temperature. While it has been possible to determine only rates of solubilization with popcorn polymer, rates of bond scission have been determined for the thermal decomposition of polystyrene prepared under the same conditions as the popcorn polymer (5). The activation energy, evaluated from these rates is 38.2 kcal. per mole. This value is in good agreement with the value of 37.2 kcal. per mole obtained by extrapolating the curve in Fig. 8 to zero butadiene content.

Further evidence that the activation energies inferred from the rates of solubilization are in fact those for the bond scission process involved, is furnished by the results shown in Fig. 9. In this figure the curves relating the rate of change of swelling index and the rate of solubilization do not coincide for polymers of different butadiene contents, showing that the relation between these two rates is dependent upon the butadiene content. For a given polymer, however, the relation is seen to be independent of temperature. This suggests that the relation between each of these rates and the rate of bond scission upon which they both depend is also independent of temperature.

The relation between the activation energy and the butadiene content shown in Fig. 8 is given by the expression,

$$\begin{aligned} \triangle E &= E - 37.3 \text{ kcal. per mole} \\ &= 0.00173 \text{ (mole \% butadiene)}^{2.6} \end{aligned}$$

The fact that $E$ increases as the 2.6 power of the butadiene content of the polymer and that the rate of decomposition decreases correspondingly as shown in Fig. 7 might be interpreted in support of the view that bonds involving butadiene are particularly significant in maintaining the insolubility of the network, i.e., that the more highly cross-linked the polymer, the more difficult it is to solubilize. This view is contradicted, however, by the results in Fig. 6 where it is seen that the plot of log (90 − % sol) against time remains linear while the swelling index of the insoluble polymer increases as much as tenfold. The rate of solubilization of popcorn of a given butadiene content would then appear to be independent of the degree of cross-linking, of which the swelling index is presumably an indication. This observation suggests very strongly that solubilization occurs by random cleavage of bonds in the polymer, without cross-links playing a particularly significant role in the process.

The decrease in the rate of decomposition with increasing butadiene content of the polymer would then be due only to an increase in the strength of the bonds present, reflected in an increased activation energy for their scission, and not to structural changes in the network. This might possibly be a result of the accompanying decrease in the number of phenyl groups present. By analogy with the influence of such groups in stabilizing free radicals of the triphenylmethyl type (6), a decrease in the number of phenyl groups in the polymer network might be expected to permit less stabilization of the free radicals which are presumably the immediate products of bond scission in the polymer. This would be reflected in an increased activation energy for the process, which is in fact observed.

It is interesting to compare the effect of butadiene in the network with the effect of solvent on reactions in homogeneous solution. It is well known that the rates and activation energies of such reactions may be profoundly influenced by the nature of the solvent medium, without the solvent being involved in the reaction itself. When the structural features of a reaction

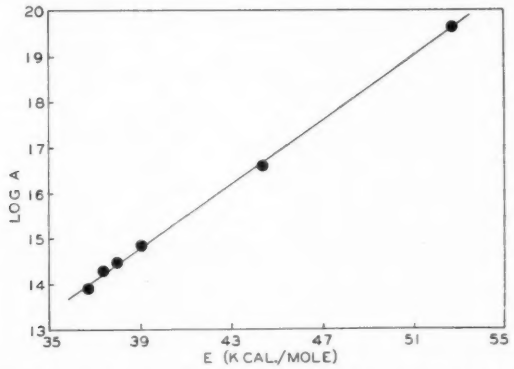


FIG. 10. *Relation between log A and E for the thermal decomposition of popcorn polymers of different butadiene contents.*

remain unaltered in a series of different solvents, a linear relation between log $A$ and $E$ for the reaction in these solvents is often obtained. A similar relation is observed in the corresponding plot for the decomposition of popcorn polymers of different butadiene contents, as shown in Fig. 10.

The significance of this relation for solution reactions has been discussed by various authors (2, 3, 8, 9). Alternative interpretations, suggested by these authors, all imply that such a relation is to be expected when the effect of the solvent is to influence the activation energy of the reaction, without altering its structural features.

It seems reasonable to conclude by analogy that the influence of the butadiene in the polymer is primarily to alter the strength of the bonds in the network. The rate of solubilization of popcorn polymer is then determined only by the activation energy of the bond scission process and is independent of the structural features of the reaction such as the degree of cross-linking. This is in accord with the conclusion previously noted.

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# ON THE O–O BOND ENERGY IN HYDROGEN PEROXIDE[1]

By Paul-A. Giguère


## Abstract

The valence-state energy of the oxygen atom, calculated recently by Pauling, agrees with the lower value, 35 kcal. per mole, for the O–O bond energy. A critical review of the question is presented.


Various estimates, some differing almost by a factor of two, have been made thus far for the energy of the O–O single bond. Although it is perfectly legitimate to discuss measurable properties, such as bond length and force constant, in relation to bond energies, it must be remembered that the quantity considered here is not susceptible of experimental verification without ambiguity. Therefore the whole question is a rather formal one.

The first calculation of the O–O bond energy by Pauling (9) was made from the heat of dissociation of gaseous hydrogen peroxide into its elements in the standard state (cf. Appendix) on the assumption that the O–H bond energy in that compound is the same as in $H_2O$. Thus he obtained a value, 34.9 kcal. per mole, which, like the corresponding one for the N–N bond, 23.6 kcal., was remarkably low by comparison with those previously found for the C–C bond, 58.6 kcal., and the F–F bond, 63.5 kcal. (These last two values, also, are now considered uncertain.) Furthermore, as pointed out by Rice (11), it was much smaller than the S–S bond energy in contradiction with the general rule that smaller atoms are bound more strongly than bigger ones. This exception was made less surprising by the smaller electron affinity of OH than that of SH (11). However, the large energy difference between the O–O and the C–C bond energy remained unexplained.

The assumption of identical energy of the O–H bond in $H_2O_2$ and in $H_2O$ was challenged by Skinner (13). On the basis of the nonequivalence of resonating structures he selected an arbitrary value, 102 kcal., about the same as the dissociation energy of the $-OH$ radical (2). This obviously led to an O–O bond energy equal to the dissociation energy of hydrogen peroxide, 52 kcal. (cf. Appendix). In support of his views he quoted the results of semiempirical quantum-mechanical calculations reported by Russian authors for the O–O bond energy in $H_2O_2$, 55 kcal. (14), and in the $\bar{O}$–$\bar{O}$ ion, 53 kcal. (8). However, on close examination the former estimate is found to rest solely on an extension of the empirical isoelectronic principle. As to the value for the $\bar{O}$–$\bar{O}$ ion, it refers in fact to the dissociation energy, not to the conventional bond energy.

That the contention of Skinner was specious and could just as well serve to support the opposite view was argued by Glockler and Matlack (6), who

1 *Manuscript received September 26, 1949.*
*Contribution from the Department of Chemistry, Laval University, Quebec, Que.*

pointed out that both $H_2O$ and $H_2O_2$ have four possible resonating structures whereas the –OH radical has only two. Comparison of the O–O distance with the corresponding bond energy in a number of molecules led these two authors to prefer Pauling's estimate over the larger one of Skinner.

Finally, in a recent article dealing at length with this question, Walsh (15) has cited a number of reasons in favor of a value even higher than that of Skinner, namely 64 kcal. He criticizes Glockler and Matlack's relationship of dissociation energies of excited molecules vs. bond lengths as not being valid for estimating bond energies. The gist of his theory is that the more polar a given bond, the weaker it is; since the O–H bond is very likely more polar in $H_2O_2$ than in the $-OH$ radical it should be correspondingly weaker. Therefore he chooses a value of $\sim 96$ kcal. for the O–H bond energy in $H_2O_2$ as compared with $\sim 100$ in $-OH$ (2) and $\sim 110$ in $H_2O$ (12). As confirmation of this he mentions: (*a*) the O–H distance, $1.01 \pm 0.03$ Å, in $H_2O_2$ reported previously by the present author (3); and (*b*) the force constant, $k_{(O\text{-}H)} = 6.5 \times 10^5$ dynes per cm., obtained from the infrared spectrum of $H_2O_2$ by Bailey and Gordon (1). Now the value $1.01 \pm 0.03$ Å was mentioned erroneously, in a prepublication note, as being the O–H distance used for calculating theoretical intensity curves for the electron diffraction of $H_2O_2$. It was never corrected officially because in the original publication of this investigation (5) it was stated quite plainly that the calculations were done with the assumed parameter $r_{(O\text{-}H)} = 0.97$ Å. (The unfortunate note was reported in Chemical Abstracts four years after it had been originally communicated.) At any rate it is well known that, because of their low scattering power, hydrogen atoms cannot in general be located accurately by electron diffraction, except in molecules, such as $B_2H_6$ and $CH_4$, which contain several times as many hydrogens as heavier atoms.

On the other hand, a recent investigation of the infrared spectrum of hydrogen peroxide (4) indicates that the frequency found by Bailey and Gordon for the O–H vibration in that molecule really belonged to the spectrum of the liquid, not to that of the vapor as was believed. The formation of hydrogen bonds is responsible for the shift from 3590 $cm.^{-1}$ in the vapor to about 3400 $cm.^{-1}$ in the liquid. Therefore the bond force-constant for O–H in $H_2O_2$ is $7.1 \times 10^5$ dynes per cm., which corresponds to a bond length of 0.98 Å (Badger's rule). In addition, high-dispersion studies (4, 16) of the second and third harmonics of this same band have made possible a calculation of the rotational constants of the molecule. Although the experimental data are not sufficient to enable an exact determination of each moment of inertia, because of the low symmetry of the molecule, the spectroscopic values agree best with those calculated for a model with an O–H distance of 0.97 to 0.98 Å. Thus it appears that this bond length is approximately the same in $H_2O_2$ as in the –OH radical (7). The "strong grounds" mentioned by Walsh in support of his line of argument are in fact nonexistent, and the influence of increased polarity on bond strength must have been exaggerated in this case.

The O–H bond length in hydrogen peroxide is not yet known with enough accuracy to be of great significance in the present discussion, let alone the validity of a close correlation between that quantity and the bond energy. The O–H frequency difference between $H_2O_2$ and $H_2O$ may well be due mainly to the difference in reduced masses rather than to a change in bond polarity. (The force constant reported above is only a first approximation, as it was not obtained from secular equations representing the potential function of the molecule as a whole.) Therefore the reasons for preferring one particular value for the O–H bond energy in $H_2O_2$ are still mostly speculative in nature, and the experimental evidence adduced in that connection remains far from compelling.

Recently Pauling (10) has calculated a valence-state energy of the bivalent oxygen atom by four different methods which yield an average value, 17 kcal., presumably reliable to about 1 kcal. Following one of his schemata, if the assumption is made that in $H_2O_2$ the energy required for removing the first hydrogen atom be equal to that for the second hydrogen atom, then the O–O bond energy in that molecule must be less than its dissociation energy by the amount of the valence-state excitation energy of the oxygen atom, i.e., $52 - 17 = 35$ kcal. Although the above schema does not constitute an independent determination of the valence-state energy of the oxygen atom it adds to the internal evidence in favor of the original assumption made by Pauling.

## Acknowledgment

The author is indebted to Dr. Verner Schomaker of the California Institute of Technology, Pasadena, for a helpful discussion.

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(The Appendix follows on the next page.)

## Appendix

The most recent data contained in the "Tables of Selected Values of Chemical Thermodynamic Properties" issued at irregular intervals since 1948 by the National Bureau of Standards, Washington, D.C., lead to the following values for the heat of decomposition (*A*), the heat of formation (*B*), and the heat of dissociation (*C*) of hydrogen peroxide:

| | | |
|---|---|---|
| | $H_2O_2(l) = H_2O(l) + \frac{1}{2} O_2(g)$ | −23.47 kcal. per mole |
| | $H_2O_2(g) = H_2O_2(l)$ | −13.01 " " " |
| | $H_2O(l) = H_2O(g)$ | 10.51 " " " |
| (*A*) | $H_2O_2(g) = H_2O(g) + \frac{1}{2} O_2(g)$ | −25.97 " " " |
| | $H_2O(g) = H_2(g) + \frac{1}{2} O_2(g)$ | 57.80 " " " |
| (*B*) | $H_2O_2(g) = H_2(g) + O_2(g)$ | 31.83 " " " |
| | $O_2(g) + H_2(g) = 2OH(g)$ | 20.12 " " " |
| (*C*) | $H_2O_2(g) = 2OH(g)$ | 51.95 " " " |

On the basis of these data the original schema of Pauling (9) would give 33.2 kcal. for the O–O bond energy in $H_2O_2$.

# THE SYNTHESIS OF *dl*-ANONAINE[1]

By Léo Marion, Lionel Lemay, and Robert Ayotte


## Abstract

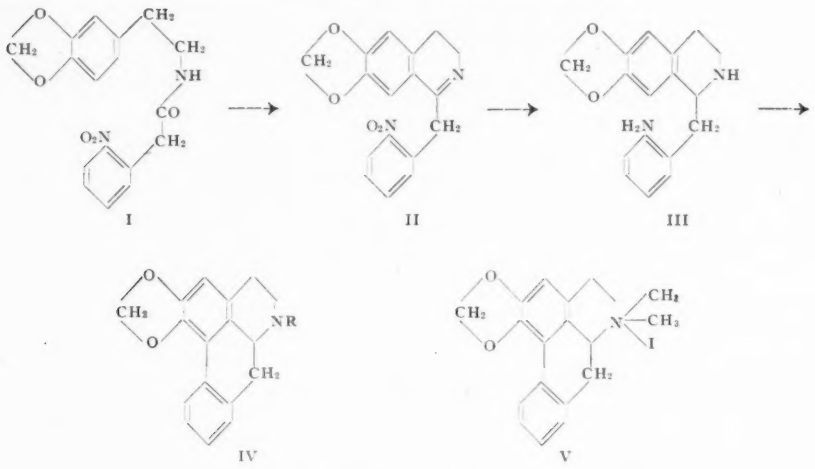
The methylenedioxy-aporphine whose structure had been assigned to anonaine has been synthesized from the amide resulting from the condensation of β-3,4-methylenedioxy-phenylethylamine and *o*-nitrophenylacetyl chloride. The amide was cyclized to the corresponding dihydroisoquinoline, the hydriodide of which was reduced and the product transformed to *dl*-anonaine by the Pschorr ring closure reaction. The synthetic base on methylation was converted to *dl*-roemerine methiodide. A comparison of the properties of the derivatives obtained from anonaine and from roemerine, the structure of which is known, supplies strong evidence in favor of the validity of the structure assigned to anonaine.


Anonaine, an alkaloid isolated from *Anona reticulata* L. (7) and *Anona squamosa* L. (6, 8), is a secondary, levorotatory base having the empirical formula $C_{17}H_{15}O_2N$ (1). The course of the Hofmann degradation of the base and the nature of the products to which it gave rise led Barger and Weitnauer (1) to assign to anonaine the aporphine structure IV(R = H). Nevertheless, the vinyl-methylenedioxy-phenanthrene obtained as a product of the Hofmann degradation of anonaine had never been synthesized, and consequently the position occupied by the methylenedioxy group in it and in the original base remained uncertain. To complete their proof of structure Barger and Weitnauer (1) attempted the synthesis of the compound of structure IV(R = H). However, they succeeded neither in crystallizing nor in resolving their synthetic product. They further attempted to synthesize the corresponding N-methyl-derivative IV(R = $CH_3$), but again obtained a product that they failed either to crystallize or to resolve. The same authors also converted naturally occurring anonaine to its N-methyl-derivative by methylation and claimed this derivative to be amorphous. The N-methyl-derivative IV (R = $CH_3$), now known to be the alkaloid roemerine (3, 4), has since been synthesized (5) and is both crystalline and readily resolvable (5). Consequently, the results of the work of Barger and Weitnauer (1) afford little confirmation for the structure of anonaine. A new attempt has, therefore, been made to synthesize the compound of formula IV(R = H).

The method employed was, with few modifications, essentially that of Barger and Weitnauer (1). Homopiperonylamine was condensed with *o*-nitrophenylacetyl chloride and the resulting amide I cyclized to 1-(*o*-nitrobenzyl)-6,7-methylenedioxy-3,4-dihydroisoquinoline (II) by the Bischler–Napieralsky reaction. Reduction of II with zinc and hydrochloric acid to 1-(*o*-aminobenzyl)-6, 7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (III) followed by the Pschorr ring closure gave a small yield of a base hydrochloride from which the crystalline base IV(R = H) was readily obtained. Attempts to resolve the synthetic base with optically active tartaric acid did not prove satisfactory

1 *Manuscript received September 14, 1949.*

*Contribution from L'Institut de Chimie, University of Montreal, and the Division of Chemistry, National Research Laboratories, Ottawa, Canada. Issued as N.R.C. No. 2061.*




and no other acids were used because of paucity of material. However, the synthetic base showed the recorded color tests (1) of naturally occurring anonaine and on treatment with methyl iodide gave rise to the methiodide of the N-methyl-derivative (V) identical with *dl*-roemerine methiodide (5). The identity of these two quaternary salts supplies proof of the validity of structure IV(R = H) for anonaine, if considered in the light of the further agreement in melting points and other properties between the products of the Hofmann degradation of *l*-anonaine and those of the similar degradation of roemerine as shown in Table I.

TABLE I

COMPARISON OF DERIVATIVES OF ANONAINE AND ROEMERINE

| Compound | Natural *l*-anonaine (1) m.p.* °C. | Natural *l*-roemerine (3,4) m.p.* °C. | Synthetic *l*-roemerine (5) m.p.† °C. |
|---|---|---|---|
| N-methylanonaine methiodide | Needles, 217° | Needles, 215-216° | Needles, 224.5° |
| Des-dimethylanonaine | Needles, 87-90° | Needles, 73-74° | Prisms, 81° |
| Des-dimethylanonaine methiodide | Platelets, 270.5° | Needles, 274-275° | Needles, 280° |
| 1-Vinyl-3,4-methylenedioxy-phenanthrene | Needles, 87° | Needles, 86-87° | |
| 3,4-Methylenedioxy-phenanthrene-1-carboxylic acid | Needles, 240° | Needles, 263-264° | |
| 3,4-Methylenedioxy-phenanthrene picrate | Red, 168° | Red, 167-168° | |

**Uncorrected.* †*Corrected.*

## Experimental

The starting materials were prepared according to methods previously described in the literature (5).

*1-(o-Nitrophenylaceto)-β-3,4-methylenedioxy-phenylethyl amide (I)*

This amide was obtained from the condensation of homopiperonylamine and *o*-nitrophenylacetyl chloride by known procedures (2, 5). The product, recrystallized from chloroform–methanol, consisted of small colorless needles melting at 127.5° C.* (The melting point 120° C. given by Marion and Grassie (5) is an error.) Yield, 62%. Calc. for $C_{17}H_{16}O_5N_2$ : C,62.19; H,4.88; N,8.54%. Found: C,62.20; H,4.84; N,8.33%.

*1-(o-Nitrobenzyl)-6,7-methylenedioxy-3,4-dihydroisoquinoline (II)*

This substituted dihydroisoquinoline was produced from the amide I by the modified Bischler–Napieralsky reaction described by Barger and Weitnauer (1). To the amide (5.0 gm.) dissolved in chloroform (20 cc.), phosphorus oxychloride (15 cc.) was added and the solution allowed to stand at room temperature for five days. The chloroform and excess phosphorus oxychloride were distilled under reduced pressure, the residual gum was dissolved in a little acetone, and the solution poured into dilute (1 : 1) hydrochloric acid (100 cc.). The insoluble material was filtered, dissolved in the minimum volume of acetone, and again poured into dilute hydrochloric acid (100 cc.). This solution was filtered and the combined filtrates filtered through a thin layer of charcoal. The resulting aqueous solution was alkalized with sodium hydroxide which caused the precipitation of the crystalline base. After recrystallization from methanol, the base consisted of brownish yellow flakes melting at 164.5° C. Yield, 79.5%. Calc. for $C_{17}H_{14}O_4N_2$ : C,65.80; H,4.52; N,9.03%. Found: C,65.97,66.12; H,4.61,4.33 : N,8.76,8.90%.

*1-(o-Aminobenzyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (III)*

The substituted dihydroisoquinoline II (5.5 gm.) was dissolved in hot dilute hydrochloric acid (240 cc.; made up of one part of concentrated acid to two of water) and to the vigorously stirred solution, powdered zinc (24 gm.) was added gradually over a period of 30 min. The solution was then cooled, filtered, alkalized with ammonium hydroxide, and extracted with three portions of ether. The combined ether extract was dried over potassium hydroxide pellets and distilled on the steam bath to remove the solvent. The residual oily base was immediately dissolved in a mixture of methanol and ether and the resulting solution saturated with dry hydrogen chloride. A crystalline dihydrochloride separated which, after recrystallization from a mixture of methanol and acetone, consisted of fine, colorless needles melting at 257° C. Yield, 75%. Calc. for $C_{17}H_{20}O_2N_2Cl_2$ : C,57.46; H,5.63; N.7.89; Cl,20.00%. Found: C,56.32,56.50; H,5.78,5.83; N,7.79,7.71; Cl,20.04%.

* *All melting points are corrected.*

*dl-Anonaine* (*IV*, $R = H$)

The above dihydrochloride (1.0 gm.), dissolved in 2 *N* sulphuric acid (10 cc.) and methanol (10 cc.) was diazotized at 0° C. with a solution of sodium nitrite (0.374 gm.) in water (2 cc.). The solution was maintained at 0° C. for 15 min. and subsequently heated on the steam bath for one hour. To the hot solution, concentrated hydrochloric acid (1.4 cc.) and powdered zinc (0.56 gm.) were added and the mixture kept on the steam bath for one hour. The supernatant liquor was then decanted and the residual zinc washed by decantation with several portions of hot water. The combined, cooled decantate was alkalized with ammonium hydroxide and the precipitated base extracted with ether. The ether extract was dried over anhydrous sodium sulphate and evaporated to dryness. The base obtained from several runs was distilled *in vacuo*; it consisted of a yellowish thick oil, b.p., 185° to 195° C. (0.05 mm.). It was dissolved in ether, the solution saturated with anhydrous hydrogen chloride, and the precipitated salt filtered and washed with ether. After repeated recrystallization from methanol–acetone, pure *dl*-anonaine hydrochloride was obtained as fine colorless needles melting at 295° C. The average yield of this reaction was only 2.5%. Calc. for $C_{17}H_{15}O_2N.HCl$ : C,67.66; H,5.31; Cl,11.77%. Found: C,67.52,67.63; H,5.17, 5.27; Cl,11.86,12.28%.

*dl*-Anonaine hydrochloride was dissolved in water, the solution alkalized with ammonium hydroxide and thoroughly extracted with ether. The combined ether extract was dried over potassium hydroxide pellets and distilled on the steam bath to remove the solvent. It left a gummy residue which was dissolved in a small volume of absolute ether. After several weeks in the refrigerator this solution deposited a crop of small prisms of slight yellowish color and melting at 116.5° C. *l*-Anonaine melted at 122° to 123° C., uncorrected (1). Calc. for $C_{17}H_{15}O_2N$ : C,76.96; H,5.65; N,5.28%. Found: C,76.90,76.97; H,5.74,5.71; N,5.21%.

*dl*-Anonaine formed a *d*-tartrate crystallizing from ethanol as clusters of fine colorless needles melting at 249° to 250° C. (dec.). Repeated fractional recrystallization of this salt failed to effect any separation into the optical isomers of the base. The base recovered from the recrystallized tartrate melted at 120.5° C.

*N-Methyl-dl-anonaine Methiodide* (*V*)

*dl*-Anonaine (0.2 gm.) was added to water (2 cc.) and methyl iodide (1 cc.) and the mixture refluxed gently during five hours. The mixture was evaporated to dryness under reduced pressure and the crystalline residue recrystallized from aqueous acetone. The product consisted of small, yellow prismatic needles melting at 224.5° C., either alone or in admixture with an authentic sample of *dl*-roemerine methiodide (5).

## Acknowledgment

The authors acknowledge with gratitude their indebtedness to the National Research Council for the award of a Studentship to one of them (R.A.).

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# OPTICAL STABILITY IN BIPHENYL, PHENYLPYRIDYL, AND BIPYRIDYL COMPOUNDS[1]

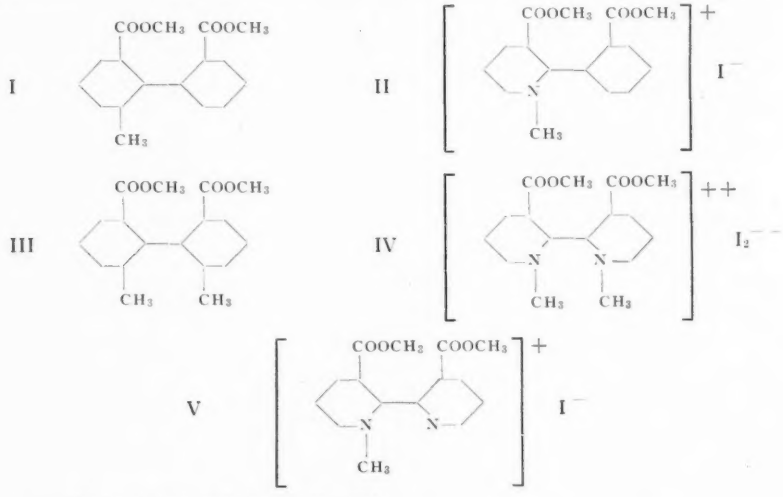
By D. Aziz and J. G. Breckenridge


## Abstract

Comparable ortho-substituted compounds of the biphenyl, 2-phenylpyridyl, and 2,2′-bipyridyl type have been synthesized and resolved, and the resistance to racemization determined. The results are as would have been predicted on geometrical considerations only, the compounds containing nitrogen atoms in the rings not behaving in any abnormal manner.


One of the more interesting aspects of the phenomenon of asymmetry in molecules due to restriction of rotation about a single bond has been the correlation between the apparent overlapping of the blocking groups and the resistance of the optical isomers to racemization. This point has been investigated mainly by Adams and coworkers, and summarized by Shriner and Adams (12). In general, the correlation is good, but there remain certain points not yet adequately explained by theory, particularly those concerned with the effect of other substituent groups not directly responsible for the blocking effect. Attention has been directed almost entirely to derivatives of biphenyl containing a variety of groups substituted in the ortho positions, and little work has been done on comparable phenylpyridines and bipyridyls; in fact, the situation with regard to bipyridyls is somewhat confused.

In the present work, we have prepared derivatives of biphenyl, phenylpyridine, and bipyridyl, in which the blocking groups are identical but




[1] *Manuscript received August 23, 1949.*
*Contribution from the Department of Chemical Engineering, University of Toronto, Toronto, Ont. From a thesis submitted by D. Aziz in partial fulfilment of the requirements for the Ph.D. degree in the University of Toronto.*

attached either to a carbon or a nitrogen atom in the ring. The particular compounds chosen for investigation were: 2,2′-dicarbomethoxy-6-methylbiphenyl (I), methyl 2,3-dicarbomethoxyphenyl-2-pyridinium iodide (II),2,2′-dicarbomethoxy-6,6′-dimethylbiphenyl (III), 1,1′-dimethyl-3,3′-dicarbomethoxy-2,2′-bipyridinium diiodide (IV), and 1-methyl-3,3′-dicarbomethoxy-2,2′-bipyridinium iodide (V).

It has been shown by Schomaker and Pauling (11) that the interatomic distances in pyridine are almost the same as those in benzene, and Gillam, Hey, and Lambert (7) have compared the absorption spectra of biphenyl and phenylpyridines and found the bond joining the rings to be of the same nature throughout. Thus compounds I and II, and III and IV, should show practically the same overlapping of the blocking groups, and unless some other effect is introduced by the fact that II and IV are ionic, we would expect that the stability to racemization of I would be of the same order of magnitude as that of II (and similarly for III and IV). In the case of compound V the situation is somewhat different, in that one of the blocking groups is the nitrogen corner of the pyridine ring. It may be compared to II, in which the corresponding position is occupied by a carbon atom with a hydrogen atom attached. It might be expected that the absence of the hydrogen atom of atomic radius approximately 0.3 Å. would result in much lower optical stability for V compared to II.

The preparation of I was first attempted by means of an Ullmann reaction between methyl 2-iodobenzoate and methyl 2-iodo-3-methylbenzoate, following the procedure recommended by Fanta (5), with subsequent hydrolysis of the mixture and fractional crystallization of the mixed acids, but this method did not give the desired product in a pure state. It was finally prepared by oxidation of 4-methylphenanthrenequinone to the diacid, which was resolved by means of morphine and then esterified, the dextro-form of I resulting. (In this and subsequent cases, the direction of rotation refers to that of a methanol solution of the substance.) It should be stated that 4-methylphenanthrenequinone is reported by Haworth (8) to have a melting point of 187° C., whereas our product, from several preparations and after repeated purifications, had a melting point of 167° C*. In addition, the quinoxaline derivative had a melting point of 161° C., while Haworth reports the melting point as 177° C. We feel confident of the purity and identity of our substances, and work is in progress to explain this discrepancy.

Compound II was prepared as described by Breckenridge and Smith (3), the dextro-form being obtained. Compound III was prepared by esterification of dextro 6,6′-dimethylbiphenyl-2,2′-dicarboxylic acid, previously reported by Bell (2). Compounds IV and V were prepared by oxidation of 1,10-phenanthroline to the diacid, esterification, conversion to the iodides, and resolution by silver α-bromocamphor-π-sulphonate.

**All melting points corrected against known standards.*

In order to measure the relative racemization rates of the substances, a solvent was necessary which would dissolve all the substances at room temperature, and could be heated to a high enough temperature to effect racemization at an appreciable rate. A variety of solvents was tried, including methanol, dioxane, and 1,1,2,2-tetrachlorethane, and the one finally chosen was ethylene glycol monomethylether (Methyl Cellosolve). Experiments were tried using a jacketed polarimeter tube, but the rates of racemization (of I and II) were too slow for the temperatures possible, and the method adopted was to reflux the solution of the substance, cooling at intervals, and taking the polarimetric readings at room temperature.

The results of the racemization experiments may be summarized as follows: compound I racemized in approximately 30 hr., the values following the unimolecular law, and the half-life value being 336 min.: compound II behaved in a similar manner, the half-life value being 353 min.: compounds III and IV were stable as regards racemization for as long as polarimetric readings could be taken: compound V racemized in approximately 30 min., the half-life being about 10 min. The results for compounds I and II are shown graphically in Fig. 1, in which the observed rotations are plotted on a logarithmic scale.

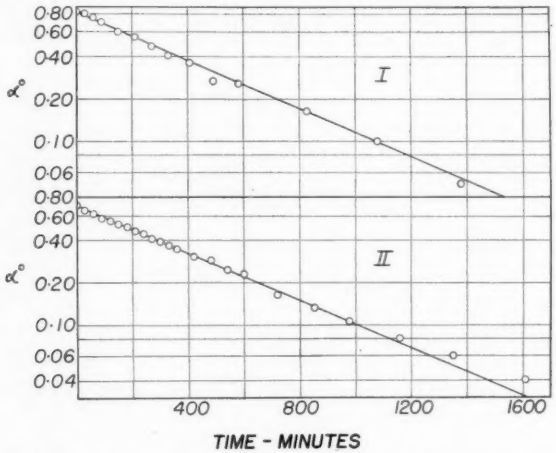



FIG. 1. *Racemization of I and II at 125° C.* ($\lambda = 5461$ Å., $t = 25°$ C., $c = 2.29$ *for I,* $c = 1$ *for II*).

The experimental results evidently agree with the predictions made above, and, in addition, this is the first case of which we are aware of resolution of a biphenyl-type compound in which one of the ortho-positions is occupied by a nitrogen atom in a ring. The case of the two bipyridyl derivatives (IV and V) is interesting in view of previous work on this type: Woodruff and Adams (14) prepared and resolved 6,6′-diphenyl-3,3′-bipyridyl-2,4,2′,4′-tetracarboxylic acid, which racemized much more readily than would have been expected for a biphenyl with comparable overlapping of the blocking

groups. This was attributed to the effect of the tertiary nitrogens in reducing the effective size of the blocking carboxyl groups. On the other hand, Brydowna (4) obtained two salts with different rotations from 2,3′-bipyridyl-2′,3-dicarboxylic acid, which might have been due to a partial resolution. Biphenyl-2,2′- dicarboxylic acid is, of course, not resolvable, and if in fact a partial resolution of Brydowna's compound was achieved, it might conceivably have been due to the ring nitrogen in the ortho position exerting a blocking effect out of all proportion to its apparent size. In the present work, the fact that compound V racemized very readily compared to II seems to show that the ring nitrogen is behaving in a normal manner.

## Experimental

*Compound I*

4-Methylphenanthrene was prepared according to Haworth (8), with slight modifications in some of the stages, as recommended by Fieser and Peters (6), Martin (10), and Bachmann and Egerton (1). The product was distilled *in vacuo* (b.p. 170° C. at 0.2 mm.), and crystallized from ethanol, the final product having a melting point of 52° to 52.5° C. The methylphenanthrene was oxidized to 4-methylphenanthrenequinone by chromic acid in acetic acid, and the quinone purified through the sodium bisulphite addition compound and recrystallized from ethanol, orange crystals, m.p. 167° to 167.2°C., being produced. Calc. for $C_{15}H_{10}O_2$ : C, 81.1; H, 4.54%. Found: C, 81.2, 81.1; H, 4.42, 4.62%. On reaction with *o*-phenylenediamine the quinoxaline was formed in quantitative yield, and had a melting point of 160.5° to 161° C. Calc. for $C_{21}H_{14}N_2$ : C, 85.7; H, 4.80; N, 9.53%. Found: C, 85.5; H, 4.84; N, 9.77%. The oxidation of the quinone to the diacid was carried out according to the procedure of Linstead and Walpole (9). The quinone (5.5 gm.) in 16 ml. glacial acetic acid was mixed with 50 ml. 6% hydrogen peroxide, and the mixture heated under reflux until a steady stream of bubbles was evolved. The heating was continued for three hours, at the end of which time the quinone color had disappeared. The solution was made alkaline, filtered, and acidified, and the resulting precipitate crystallized from aqueous methanol, white crystals, m.p. 228° to 229° C., being produced. Calc. for $C_{15}H_{12}O_4$ : C, 70.3; H, 4.72%. Found: C, 69.6; H, 4.43%.

The resolution of the diacid was carried out as follows: 2.72 gm. (0.1 mole) of the diacid and 0.1 mole morphine hydrate were dissolved in 50 ml. hot ethanol, and on cooling the solution a yield of 2.5 gm. white crystals, m.p. 208° C., was obtained. Calc. for $C_{32}H_{31}O_7N.H_2O$ : C, 68.7; H, 5.94; N, 2.50%. Found: C, 69.2, 68.9; H, 5.90, 5.89; N, 2.60%. In glacial acetic acid ($c = 1$), $[\alpha]^{23}_{5461} = -78.5°$, $[\alpha]^{23}_{5780} = -69.4°$. On decomposition of the morphine salt with cold dilute hydrochloric acid, the laevo-form of the diacid was obtained, with m.p. 228° C. after softening at 192° C. and resolidifying. In methanol ($c = 1$), $[\alpha]^{25}_{5461} = -7.73°$, $[\alpha]^{25}_{5780} = -6.95°$. The acid (0.3 gm.) was placed in a test tube fitted with a side arm, and 1.5

ml. thionyl chloride added. The tube was stoppered, and, after the mixture had stood at room temperature for two and one-half hours, the excess thionyl chloride was removed by suction, and the remaining oil treated with 5 ml. methanol and allowed to stand for two hours. The methanol was evaporated, and the resulting liquid ester dissolved in ether and washed with 0.1 *N* sodium hydroxide followed by water. The ethereal solution was clarified in the cold with carbon, the ether distilled off, and the ester recovered as a colorless oil. Calc. for $C_{17}H_{16}O_4$ : C, 71.8; H, 5.68%. Found: C, 71.8; H, 5.74%. The specific and molecular rotations for compounds I–V are listed in Table I.

*Compound II*

This was prepared as described by Breckenridge and Smith (3), the dextro-form being obtained, m.p. 159° C.

*Compound III*

The corresponding acid was prepared and resolved with morphine as described by Bell (2). The morphine salt on decomposition with ice and hydrochloric acid gave the dextro-acid, m.p. 211° to 212.5° C. In methanol ($c = 1$), $[\alpha]^{25}_{5461} = +23.2°$, $[\alpha]^{25}_{5780} = +20.1°$. Esterification of this with diazomethane resulted in some racemization, and the reaction was finally carried out with thionyl chloride and methanol, using the same conditions as in the preparation of I. The dextro-ester was a white crystalline solid, m.p. 42° C. (The racemic ester had a melting point of 100° C.). Calc. for $C_{18}H_{18}O_4$ : C, 72.5; H, 6.08%. Found: C, 72.6; H, 5.98%.

*Compound IV*

1,10-Phenanthroline was oxidized to the diacid as described by Smith and Richter (13), the product having a melting point of 250° C. This was converted to the diester with diazomethane, and the ester crystallized from methanol–ether as pale yellow prisms, m.p. 152° C. Calc. for $C_{14}H_{12}O_4N_2$ : C, 61.7; H, 4.45; N, 10.0%. Found: C, 61.6; H, 4.41; N, 9.79%. The ester was heated for one hour on the steam bath with two equivalents of dimethyl sulphate, while stirring vigorously, and the resulting brown viscous mass, which solidified on cooling, was washed with dry acetone, the dimethosulphate remaining as a white powder. Crystallization of this from methanol–ether produced white crystals, m.p. 208° C. Calc. for $C_{18}H_{24}O_{12}N_2S_2$ : S, 12.3%. Found: S, 13.0%. The dimethosulphate was dissolved in the least possible quantity of water, and excess potassium iodide added. The yellow solution deposited crystals which were recrystallized several times from methanol–ether, the product being formed as orange needles, m.p. 175° to 176° C. Calc. for $C_{16}H_{18}O_4N_2I_2$ : I, 45.6%. Found: I, 45.2%. The dimethiodide was dissolved in water and the equivalent amount of silver α-bromocamphor-π-sulphonate added, the mixture filtered, and the filtrate evaporated *in vacuo*. The product, a yellow gum, was obtained crystalline by slow

evaporation of an acetone – ethyl acetate solution, and recrystallization from acetone–ether produced white crystals, m.p. 150° to 154° C. Calc. for $C_{36}H_{46}O_{12}N_2S_2Br_2$ : C, 46.8; H, 5.11%. Found: C, 46.3, 46.8; H, 5.4, 5.2%. In methanol ($c$ = 0.5), $[\alpha]^{25}_{5461}$ = + 74.5°, $[\alpha]^{25}_{5780}$ = + 69.5°. Treatment of the camphorsulphonate salt with potassium iodide gave the dextro-form of the dimethiodide as yellow crystals, m.p. 179° to 180° C.

*Compound V*

The dimethyl ester of 2,2′-bipyridyl-3,3′-dicarboxylic acid (see above) was heated in benzene solution with one equivalent of dimethyl sulphate, the monomethosulphate coming out of solution as a white powder. This on treatment with potassium iodide gave the monomethiodide as yellow flakes, m.p. 153° to 154° C. Calc. for $C_{15}H_{15}O_4N_2I$ : C, 43.5; H, 3.65%. Found: C, 43.4; H, 3.61%. Reaction with silver α-bromocamphor-π-sulphonate gave the bromocamphorsulphonate salt as white crystals from acetone–ether, m.p. 159° to 159.5° C. Calc. for $C_{25}H_{29}O_8N_2SBr$ : C, 50.3; H, 4.89%. Found: C, 50.4; H, 4.97%. In methanol ($c$ = 0.675), $[\alpha]^{25}_{5461}$ = −273°, $[\alpha]^{25}_{5780}$ = − 206°. On treatment with potassium iodide the dextro-monomethiodide was formed, and was recrystallized from acetone–ether as yellow crystals, m.p. 136° to 137° C.

*Specific and Molecular Rotations*

These values for compounds I to V in methanol and Methyl Cellosolve are listed in Table I.

TABLE I

| Compound | Solvent | $c$ | $[\alpha]^{25}_{5461}$ | $[\alpha]^{25}_{5780}$ | $[M]^{25}_{5461}$ |
|---|---|---|---|---|---|
| I | Methanol | 1 | + 20.15° | + 17.75° | + 57.0° |
| I | Methyl Cellosolve | 2.29 | + 18.1° | + 15.95° | + 51.2° |
| II | Methanol | 1 | + 29.4° | + 24.3° | + 124.8° |
| II | Methyl Cellosolve | 1 | + 35.0° | + 28.0° | + 148.7° |
| III | Methanol | 1 | + 56.0° | + 48.5° | + 167.0° |
| III | Methyl Cellosolve | 1 | + 52.3° | + 44.3° | + 156.5° |
| IV | Methanol | 0.5 | + 15.4° | + 13.3° | + 85.0° |
| IV | Methyl Cellosolve | 0.25 | + 19.2° | + 15.4° | + 108.0° |
| V | Methanol | 0.39 | + 10.0° | + 7.75° | + 42.5° |
| V | Methyl Cellosolve | 0.57 | − 21.7° | − 20.7° | − 92.2° |

*Racemization Experiments*

These were carried out by dissolving a weighed quantity of substance in the solvent (Methyl Cellosolve, b.p. 125° C.) and making the volume up to 15 ml. After the initial rotation (at 25° C.) had been measured, the solution was heated under reflux for a suitable time, cooled, made up to the correct weight with fresh solvent if necessary, and another polarimetric reading taken. This procedure was continued until the compound had racemized or until

it was evident that racemization was negligible. The results for I and II are shown in Table II ($c = 2.29$ for I, $c = 1$ for II), the velocity constants being calculated for a unimolecular reaction.

TABLE II

| Time, min. | Compound I | | Compound II | |
|---|---|---|---|---|
| | $\alpha^{25}_{5461}$ | $k$ | $\alpha^{25}_{5461}$ | $k$ |
| 0 | 0.83 | — | 0.70 | — |
| 5 | 0.83 | 0 | 0.70 | 0 |
| 15 | 0.82 | 0.00041 | 0.68 | 0.00098 |
| 30 | 0.80 | 0.00058 | 0.65 | 0.00123 |
| 45 | — | — | 0.63 | 0.00118 |
| 60 | 0.73 | 0.00107 | 0.62 | 0.00101 |
| 75 | — | — | 0.60 | 0.00103 |
| 90 | 0.70 | 0.00095 | 0.57 | 0.00114 |
| 120 | — | — | 0.55 | 0.00100 |
| 150 | 0.60 | 0.00108 | 0.52 | 0.00099 |
| 180 | — | — | 0.49 | 0.00099 |
| 210 | 0.55 | 0.00098 | 0.46 | 0.00100 |
| 240 | — | — | 0.44 | 0.00097 |
| 270 | 0.47 | 0.00105 | 0.41 | 0.00099 |
| 300 | — | — | 0.39 | 0.00098 |
| 330 | 0.41 | 0.00107 | 0.37 | 0.00097 |
| 360 | — | — | 0.35 | 0.00096 |
| 407 | 0.36 | 0.00102 | — | — |
| 420 | — | — | 0.31 | 0.00097 |
| 480 | — | — | 0.29 | 0.00092 |
| 492 | 0.27 | 0.00114 | — | — |
| 540 | — | — | 0.25 | 0.00095 |
| 582 | 0.26 | 0.00099 | — | — |
| 600 | — | — | 0.23 | 0.00093 |
| 720 | — | — | 0.17 | 0.00098 |
| 828 | 0.17 | 0.00096 | — | — |
| 852 | — | — | 0.14 | 0.00095 |
| 978 | — | — | 0.11 | 0.00095 |
| 1080 | 0.10 | 0.00098 | — | — |
| 1158 | — | — | 0.08 | 0.00094 |
| 1350 | — | — | 0.06 | 0.00091 |
| 1380 | 0.05 | 0.00102 | — | — |
| 1608 | — | — | 0.04 | 0.00089 |
| Average value of $k$ (after $t = 30$ min.) | | 0.00103 | | 0.00098 |
| Half life, min. | | 336 | | 353 |

A second series of readings was taken on another sample of the two compounds, and the results agreed with those in Table II within the experimental error. An attempt was also made to measure the racemization rates in aqueous dioxane; in 95% dioxane compound I had a half life of 52 hr., but compound II showed signs of decomposition as well as racemization, and the solution became too highly colored to take accurate readings. From both the Methyl Cellosolve and the dioxane the racemic form of compound I was recovered as a colorless oil, which on hydrolysis gave the inactive acid, m.p. 228° C., while compound II was not readily recovered in a pure state, slight decomposition having occurred.

Compound III under the same conditions showed no evidence of racemization after heating at 125° C. for 48 hr., while compound IV retained its original rotation for two hours, at the end of which time slight decomposition had deepened the original yellow color of the solution to a point where accurate readings could no longer be taken. Compound V under the same conditions racemized very readily, the rotation falling to zero in about half an hour. Insufficient material was available to repeat the experiment, and, owing to the color of the solution, the results were only very approximate. The inactive methiodide, m.p. 149° to 152° C., was recovered. It is intended to repeat and extend the observations on compound V in the near future.

## Acknowledgment

We wish to express our thanks to the School of Engineering Research, University of Toronto, for financial aid.

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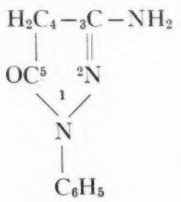
## NOTES

### Synthetic and Spectrometric Studies of Some Pyrazolones—A Correction[1]

In a recent paper (2) the ultraviolet absorption spectra of several pyrazolones were described and tautomeric bond structures were proposed for the various derivatives on the basis of ultraviolet absorption spectra, color reactions with ferric chloride, and reactions with nitrous acid. This paper included a description of several N-phenyl derivatives of 4-substituted-3-amino-5-pyrazolones prepared by the condensation of alkyl cyanoacetates with phenylhydrazine.

During the initial stages of these investigations, it was assumed that this reaction yielded 1-phenyl derivatives, and this view was supported by the close similarity of the ultraviolet absorption spectrum of the 4-methyl-N-phenyl-3-amino-5-pyrazolone derivative with that of a compound synthesized by Conrad and Zart (1) by condensation of ethyl cyanoacetate and phenylhydrazine; the structure of this compound was established by Weissberger and Porter (3) as I.



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On the basis of this structure for the N-phenyl derivatives, a self-consistent series of formulas were proposed which provided a rational explanation for the classification of the ultraviolet absorption spectra into "low intensity" and "high intensity" types, and for the direction of the displacement of the absorption maxima on acidification. These structures also accounted for the reactions of the various types of pyrazolone derivatives with ferric chloride and with nitrous acid.

Subsequent to the acceptance of this manuscript for publication, further chemical evidence was accumulated which indicated that in the N-phenyl derivatives the phenyl group was attached to the nitrogen at position 2. The structures attributed to these compounds were accordingly changed in the manuscript and certain other alterations made. As a result of these changes,

[1]*Issued as N.R.C. No. 2059.*

inconsistencies were introduced in the arguments developed in the discussion of the bond structures on pages 203 and 204 and we therefore wish to withdraw the proposed structures XX, XXI, XXII, and XXIII. Structures X and XI should also be deleted from line 9 of page 202.

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MANUSCRIPT RECEIVED SEPTEMBER 17, 1949.

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## Deuterium Exchange in Trichlorethylene[1]

Trichlorethylene-*d*, $CDCl : CCl_2$, was lately required for the synthesis of *asym*-tetrachlorethane-$d_2$, $CD_2Cl.CCl_3$ (1). It seemed probable that *sym*-tetrachlorethane-$d_2$ would be readily converted into trichlorethylene-*d* by the action of calcium hydroxide and water according to the equation:

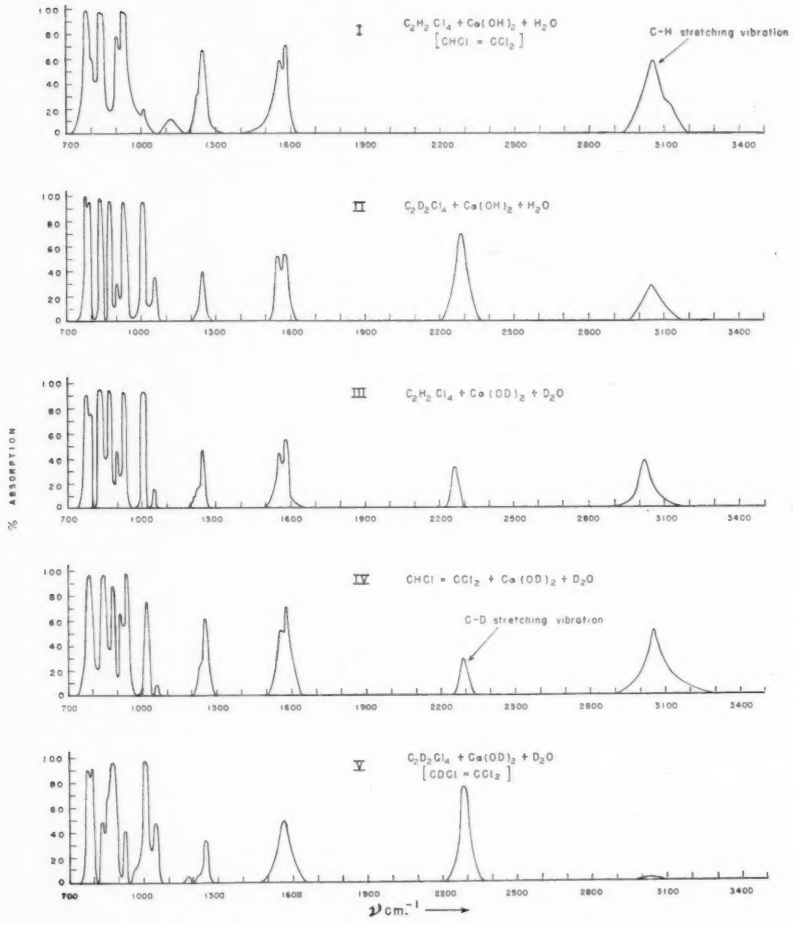
$$2CDCl_2.CDCl_2 + Ca(OH)_2 \rightarrow 2CDCl : CCl_2 + 2HDO + CaCl_2.$$

Actually, the trichlorethylene-*d* which was isolated from the reaction mixture contained a large amount of the protium compound, as shown by a comparison of its infrared absorption spectrum (II of Fig. 1) with that of pure trichlorethylene (I of Fig. 1). A mixture of the light and heavy forms was also obtained by reacting tetrachlorethane, calcium deuteroxide and deuterium oxide under identical conditions, as indicated from an examination of the infrared absorption spectrum of the product (III of Fig. 1). Exchange had evidently occurred in both cases.

There was some uncertainty whether the tetrachlorethane or the trichlorethylene was involved in the exchange. However, since dehalogenation of *sym*-tetrachlorethane-$d_2$ with zinc in a solution of 95% ethanol gave solely deuterated dichlorethylenes (2), it was considered unlikely that exchange had taken place in the present instance between the tetrachlorethane and the solvent. The matter was finally settled when it was observed that trichlorethylene itself gave a mixture of the light and heavy forms when heated in the presence of calcium deuteroxide and deuterium oxide. The infrared absorption spectrum of the product is shown in IV of Fig. 1.

Nearly pure trichlorethylene-*d* was obtained by heating *sym*-tetrachlorethane-$d_2$ with calcium deuteroxide and deuterium oxide. Its absorption spectrum is shown in V of Fig. 1.

[1]*Issued as N.R.C. No. 2056.*




To our knowledge this is the first time deuterium exchange in trichlorethylene has been reported.

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MANUSCRIPT RECEIVED SEPTEMBER 28, 1949.

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## Crystal Tests as a Means of Identifying Alkaloids

The problem of identifying alkaloids depends to some extent on the quantity of material available for testing and on the amount of extraneous material which may be present when the alkaloid is recovered from biological material such as blood, urine, or body tissues. If the material is pure and 100 μgm. or more may be used in each test for crystal, biological, or color reactions, the problem is not so serious. Indeed, when the supply is ample, melting point determinations may be made or a curve determined in the spectrophotometer. When the whole quantity for a series of determinations is of the order of 50 μgm. or even less, the above methods may not be sufficiently delicate or precise. In recovery of small amounts of alkaloid from biological material, a point may be reached where further purification entails such a loss of drug that a test which would identify the alkaloid in the slightly impure solution available would be very welcome. It is at this point that crystal tests may be most useful.

The method for obtaining crystals which was employed by Stephenson (1) when plenty of material was available and which readily lends itself to photography is the one in which solutions of the material and the reagent are mixed on a slide and are covered with a cover slip. Crystals grow slowly or rapidly, depending on the concentration of the drug, and when they have formed will give an undistorted image in the microscope for photographing. When too low concentrations of the drug are employed, crystals may not form under the cover slip.

A second method which may be employed successfully is to draw up in flattened capillary tubes some of the solution containing the drug and some of the crystallizing reagent. Crystals may form at the interface. The tube may be sealed at each end and the contents mixed by shaking. If the concentration of drug is sufficient, crystals will form; if not, since the ends are sealed and no evaporation occurs, none will appear. Photomicrography of the crystals usually shows some distortion, since the glass surfaces are not optically flat. Such long needles as those forming whenever dilute solutions of morphine are mixed with Marme's solution*, may be photographed readily in the flattened capillary. Examples of such needles are shown in Plate I, Figs 1. 2, 3, 4. The early crystals appear as fine individual needles but soon arrange themselves in a spray form, a number of needles arising from a point. The short, fine crystals which form when solutions of strychnine and gold chloride are mixed in a flattened capillary tube are frequently so distorted that they are difficult to recognize or photograph satisfactorily.

The method which is employed by a number of chemists searching for alkaloids in saliva or urine of animals is the one first employed by Charles Morgan, Chemist for the New York State Racing Association.

**Autenrieth Warren. Detection of Poisons. 6th ed. P. Blakiston's Son and Co., Philadelphia, 1928. p. 639.*

PLATE I

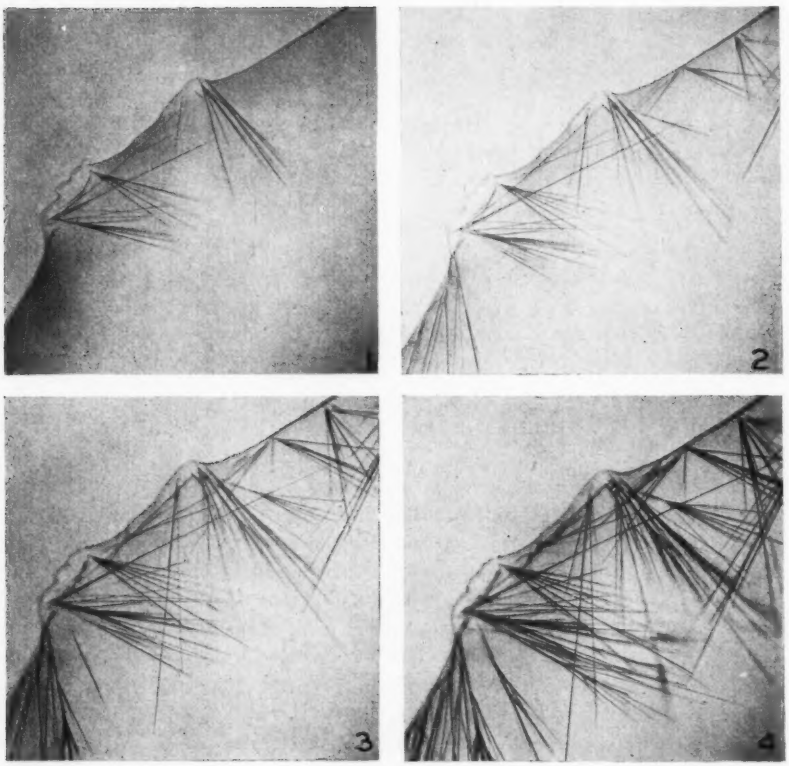


FIG. 1. *Dilute morphine solution with Marme's reagent. Fine needles form at the edge of the drop.* FIG. 2. *Crystals continue to grow fairly rapidly. (Three minutes later.)* FIG. 3. *Further growth. (Three minutes later.)* FIG. 4. *Further growth. (Three minutes later.)*

The method lends itself more readily to the detection of alkaloids in rapid routine work where many samples must be observed in a few hours. It is particularly valuable when low concentrations of the drug are present and has the advantage of keeping the solution in place and permitting two tests to be made on one slide. One microgram, or even less, of morphine may show characteristic crystals with Marme's reagent.

In this method, slides containing double depressions are employed. A small drop of the drug solution is placed in one of the depressions and to it is added a small drop of reagent. This differs somewhat from the method published by Whitmore and Wood (2, 3). The total quantity is such that the depression is about two-thirds filled by the drop. Spontaneous evaporation is permitted or the slide may be put under a fan. Concentration takes place more rapidly at the surface and the outer edges. The outer edge is examined frequently; when spontaneous evaporation is allowed, the slide may rest on the microscope platform. If crystals occur early, characteristic ones will soon form on the edge and either grow inwards or along the edge. The slide must be rotated and the whole perimeter of the drop examined, for it seems, possibly owing to the uneven mixing, that the crystals occur more readily in one spot than in another on the edge. Examination must be made very frequently; in such instances as that of identifying morphine with Marme's reagent, abundant crystals of the reagent may appear early and obscure the small crystals of morphine.

A distinct advantage of using the slides having the depression for crystal tests is that photomicrographs may be made of the crystals on the slide under the microscope and a permanent record preserved for future reference. The growth of the crystals and any changes in form as the crystals become larger, may be photographed. In Plate II, four photomicrographs are shown of crystals forming when solutions of benzedrine and platinic chloride–sodium iodide reagent* were mixed in a depression on a double depression slide, the slide being held in position on the stage of a microscope and spontaneous evaporation proceeding. A portion of the edge of the drop was focused through the microscope on a ground glass fastened to a revolving stage which held also a Leica camera with the film of the camera in the same focal place as the ground glass, above the eyepiece. When crystals appeared four minutes after the mixing and were focused on the ground glass, the camera was rotated to the position of the ground glass and a photograph was taken. This is the standard procedure for taking photomicrographs in this Laboratory. The ground glass was then substituted for the camera and when more crystals had formed and were focused on the glass, further photographing was carried out, as indicated above. An analyst familiar with this method, when informed of the reagent used, may identify an alkaloid present by a glance through the microscope at the crystals on the edge or by examination of the photomicrograph.

**Dissolve 1.8 gm. of sodium iodide in 6 cc. of water. Mix this solution with 10 cc. of a 5% solution of platinic chloride ($PtCl_4.2HCl.6H_2O$).*

PLATE II

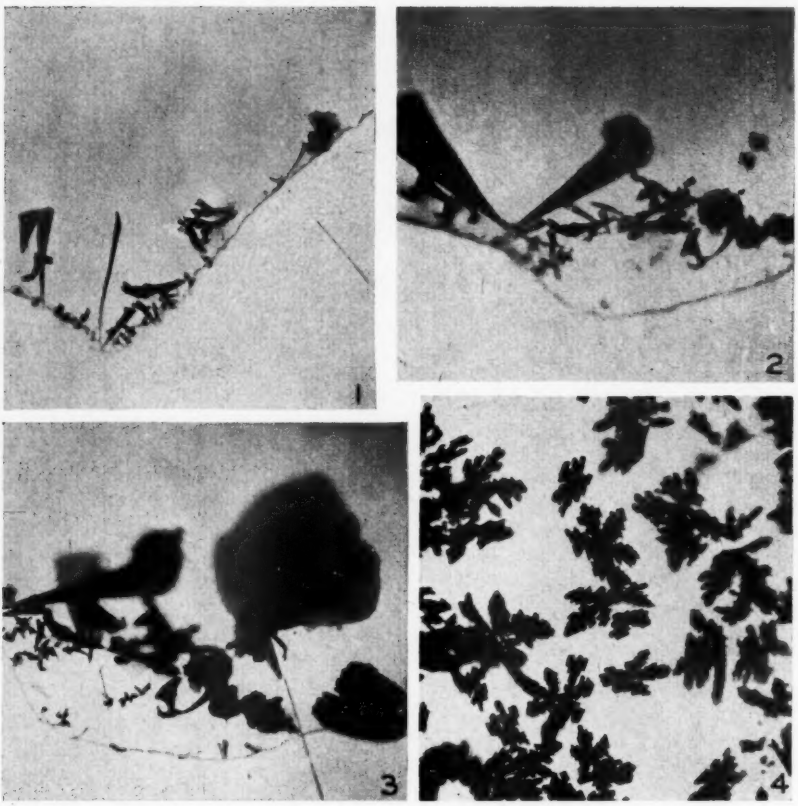


FIG. 1. *Dilute solution of benzedrine in $PtCl_2$—NaI reagent. (Four minutes.)* FIG. 2. *Two minutes later. Irregular plates become quite noticeable.* FIG. 3. *Two minutes later. Very coarse red plates quite obvious.* FIG. 4. *Strong solutions of benzedrine produce large well formed, red crystals.*

PLATE III

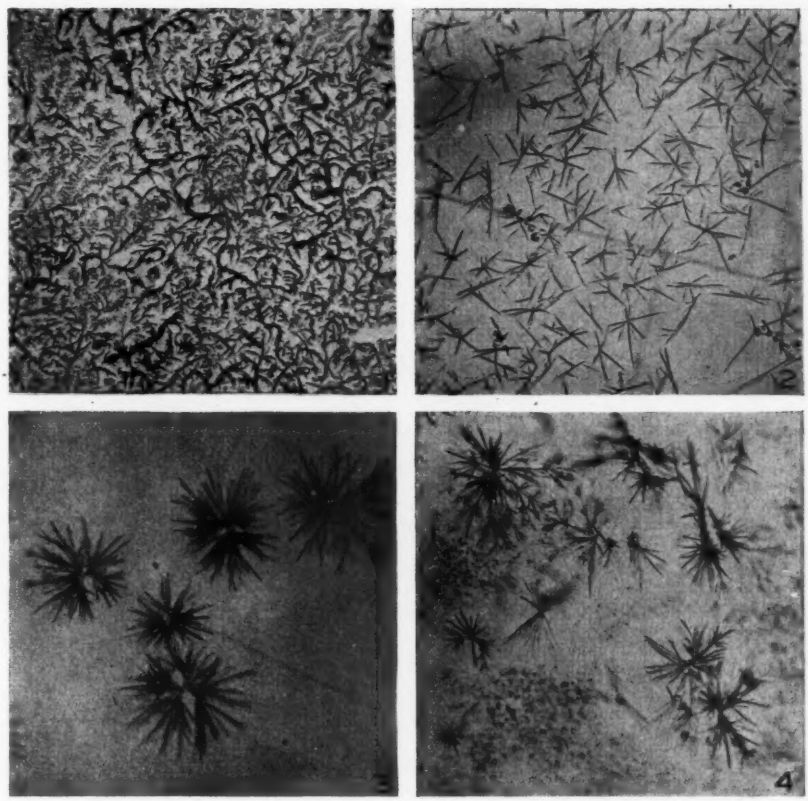

FIG. 1. *Amidone (free base). Recrystallized from ether.* FIG. 2. *Amidone with gold chloride–hydrogen iodide reagent.* FIG. 3. *Amidone with mercuric chloride reagent.* FIG. 4. *Amidone with mercuric bromide reagent.*

The above examples illustrate the change in size and appearance of crystals as they grow. Frequently only traces of an alkaloid may be in the solution tested and therefore only the earliest crystal forms will be present. The spontaneous evaporation increases the concentration of the alkaloid in the drop on the slide and frequently the later forms may become evident. It must be remembered, however, that the reagents themselves crystallize and at times obscure the crystals of the alkaloid.

In Plate III are shown four photomicrographs of crystals of a relatively new drug, amidone, made with several standard reagents. It is obvious that these entirely different crystals could serve to identify amidone.

Only by experimentation will the most satisfactory reagent for crystallizing be found. The presence of sulphuric, phosphoric, hydrobromic, or hydrochloric acid up to 25% by volume may greatly assist in the formation of characteristic crystals when gold or platinum solutions are used as the crystallizing reagents.

1. STEPHENSON, CHARLES H. and PARKER, C. E. Some microchemical tests for alkaloids; including chemical tests of the alkaloids used by C. E. Parker. J. B. Lippincott Company, Philadelphia and London. 1921.
2. WHITMORE, W. F. and WOOD, C. A. Mikrochemie ver. Mikrochim. Acta, 27 : 249. 1939.
3. WHITMORE, W. F. and WOOD, C. A. Mikrochemie ver. Mikrochim. Acta, 28 : 2. 1939.

RECEIVED
IN ORIGINAL FORM, MAY 14, 1949.
AS REVISED, OCTOBER 27, 1949.

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